



Cancer Research

Poster Session Abstracts

Abstract P5-01-08: Single dose acute toxicity and long-term biodistribution of perfluoropentane loaded iron doped silica nanoshells

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Thirty-Seventh Annual CTRC-AACR San Antonio Breast Cancer Symposium; December 9-13, 2014; San Antonio, TX

Abstract

Background: Our lab has been focusing on developing a better method of localizing non-palpable breast cancers without wire or seed localization. Perfluoropentane (PFP) loaded Fe-SiO₂ nanoshells have been developed as a color Doppler ultrasound contrast imaging agent which can act as small volume (100 ul) injectable stationary guide-marker for breast tumor resection. Preliminary experiments have demonstrated that the nanoshells can provide robust contrast for periods extending past 10 days in vivo in Py8119 epithelial breast tumor bearing mice with no adverse affect to the mice. Short-term biodistribution over 72 hours of nanoshells using In¹¹¹ labeled nanoshells demonstrated with gamma scintigraphy that intravenously dosed particles primarily accumulate in the liver but some radioactive signal can be seen in the bladder. The long imaging lifetime of these nanoshells necessitates the need to study long-term toxicity and biodistribution.

Materials and Methods: Fe-SiO₂ nanoshells and Pure SiO₂ nanoshells were synthesized via sol-gel method on polystyrene templates and then calcined to yield 500 nm hollow rigid nanoshells which were then filled with vaporized perfluoropentane. 100 ul of nanoshells at 4 mg/ml of the Fe-SiO₂ nanoshells and at a dose of 2 mg/ml of pure SiO₂ nanoshells were injected IV into healthy 8-week old Swiss white mice. The difference in mass dose was due to make the particle count between the two doses equivalent. Blood was collected weekly for serum chemistry and hematology. After 10 weeks mice were sacrificed, H&E was performed on organs of interest as well as inductively coupled plasma optical emission spectroscopy (ICP-OES) for trace silicon determination for long-term biodistribution.

Results: No significant effect due to the administration has yet been observed on the health of brain, lung, heart, kidney, liver, spleen or muscle tissue examined from these animals at a dose 4 mg/ml 100 ul of the Fe-SiO₂ nanoshells and at a dose of 2 mg/ml of pure SiO₂ nanoshells. Mouse weight steadily increased from 25.8 ± 2 grams to 30.7 ± 2.6 grams over the course of 10 weeks. Creatinine levels were detected at 0.2 ± 0.14 mg/dl indicating healthy renal function. Serum glutamic pyruvic transaminase (SGPT) was used as a measure of liver health, and SGPT values for both control (55.81 ± 6.31 U/L) and nanoshell injected mice (47.74 ± 11.04 U/L) are approximately the same over the course of 10 weeks indicating good liver health. Silicon content in mouse organs diminished over the course of 10 weeks by ICP-OES in both the Fe-SiO₂ and pure SiO₂ nanoshells.

Conclusions: No indication of toxicity was observed from a 400 ug systemically administered dose of Fe-SiO₂ nanoshells. Furthermore, the reduction of silicon content in the organs over the course of 10 weeks suggests a possible excretion pathway for silica or solid nanoparticulate materials. The efficacy in long term ultrasound contrast and high margin of safety indicates that this particle formulation is ready for phase 1 clinical trial in humans as a future method to localize nonpalpable breast cancers.

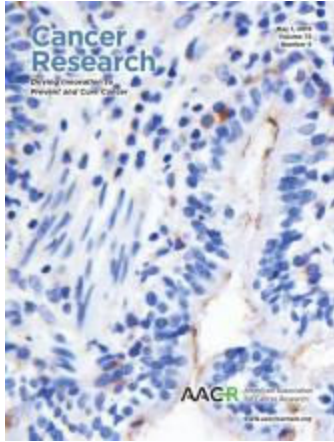
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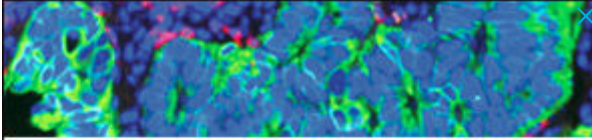
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